Project proposal for Factor VIII, Factor IX and Rare coagulation disorders SSC

Title: Chromogenic Assay versus One Stage Assay to Diagnose Women and Girls with Hemophilia A and Hemophilia A Carriers: mapping global approaches and assessing challenges

Rationale:

In hemophilia patients, one stage assay (OSA) has been considered the first-line assay to assess FVIII activity in 90% of diagnostic laboratories according to the results of published global surveys. Studies have shown that 20% to 50% of patients with mild to moderate hemophilia A have an assay-related discrepancy in FVIII:C results, wherein the OSA is two-fivefold higher than the chromogenic assay (CSA) and patients with lower CSA levels have been shown to have a more severe bleeding tendency. This can cause poor factor level to bleeding phenotype correlation and has frequently led to change in the patient's assigned hemophilia severity, in turn requiring change in treatment approaches.

The OSA: CSA discrepancy has not been well addressed in diagnosing women and girls with Hemophilia A (WGwHA) with FVIII deficiencies <40 IU/dl and symptomatic and asymptomatic Hemophilia A carriers (HAc) with FVIII >40 IU/dl. At our center, we showed that initially CSA was not obtained in all WGwHA and HAc and that CSA was discrepantly lower than OSA in a subset of WGwHA and HAc, which has led to ongoing efforts to consistently obtain CSA levels in all WGwHA and HAc. CSA may not be readily accessible or not economically feasible even if readily available in other centers caring for WGwHA and HAc across the world. In general, CSA is considered to be complicated, difficult to automate, expensive and not linear across a wide range of clotting factor activities, although with current automation options there are potential solutions to simplify the assay procedure to make it more readily available, less expensive and reliable. There is need to assess the global practice of Hemophilia providers in utilizing OSA versus CSA in diagnosing WGwHA and HAc, and to assess the challenges with doing CSA for diagnosing WGwHA and HAc, as this can impact their accurate diagnosis and optimal management.

Aim:

1. To describe current practices and perspectives of hemophilia providers worldwide in testing WGwHA and HAc in regards to using OSA and/or CSA
2. To assess if FVIII levels obtained by OSA or CSA corelate better with bleeding assessment tool (BAT) score in WGwHA and HAc.

Research questions:

1. Do hemophilia providers worldwide test WGwHA and HAc with OSA and/or CSA for confirming the diagnosis?
2. Do the Bleeding Assessment Tool (BAT) scores corelate better with FVIII level obtained with OSA or CSA in WGwHA and HAc?
3. What are the current challenges to do CSA to diagnose WGwHA and HAc, in terms of assay parameters including cost and availability?

Benefit to ISTH priorities:

Our project will potentially reveal heterogeneous clinical practices in using OSA versus CSA, reflecting the uncertainty of clinicians and challenges with assay availability and utilization for diagnosing WGwHA and HAc. We will also learn whether FVIII level obtained by OSA or CSA corelates better with BAT in and HAc. In addition, we will learn about the perspectives of hemophilia providers, the availability or lack thereof of the CSA globally and the potential under-diagnoses and under-treatment of WGwHA and HAc because of the assay-related discrepancies.

Methods:

We will perform an online international survey of hemophilia providers from across the globe, by contacting the members of the ISTH. Results will be presented at international conferences, and submitted to peer reviewed hematology/hemostasis journals.

Research team/collaborators:

Project coordination will be the responsibility of Dr Lakshmi Srivaths, Dr. Miguel Escobar and Ms. Joanna Larson PNP, at Gulf States Hemophilia and Thrombophilia Center, University of Texas Health Science Center at Houston/McGovern Medical Center, Houston, Texas. A steering board of experts with global representation will contribute to the contents of the survey questions. The names of the experts will be finalized once the project proposal is approved.

References:

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